PENDING CLAIMS

114. A method of providing a therapeutic product to a mammal, comprising introducing into the mammal a vertebrate cell which produces the therapeutic product, the cell being generated by an *in vitro* process comprising:

(a) providing a cell the genomic DNA of which comprises an endogenous gene;

(b) providing a DNA construct comprising:

(i) a targeting sequence;

(ii) an exogenous regulatory sequence;

(iii) an exon;

(iv) a splice-donor site;

(v) an intron; and

(vi) a splice-acceptor site; and

(c) transfecting the vertebrate cell with the DNA construct, thereby generating a homologously recombinant cell in which the exogenous regulatory sequence controls transcription of (b) (iii)-(vi) in addition to all exons of the endogenous gene to produce an RNA transcript that encodes the therapeutic product.

115. The method of claim 114, wherein the vertebrate cell is a primary or secondary cell.

116. The method of claim 115, wherein the primary or secondary cell is a mammalian cell.

117. The method of claim 115, wherein the primary or secondary cell is a human cell.

118. The method of claim 114, wherein the vertebrate cell is an immortalized cell.

119. The method of claim 118, wherein the immortalized cell is of mammalian origin.

120. The method of claim 118, wherein the immortalized cell is of human origin.

121. The method of claim 114, wherein the homologously recombinant cell is cultured under *in vitro* conditions which permit proliferation of the homologously recombinant cell, thereby generating a plurality of homologously recombinant cells which produce the therapeutic product.

122. The method of claim 121, wherein the therapeutic product is a protein or glycoprotein that is secreted by the plurality of homologously recombinant cells.

123. The method of claim 114, wherein the construct-derived exon comprises a CAP site.

124. The method of claim 123, wherein the construct-derived exon further comprises the nucleotide sequence ATG.

125. The method of claim 124, wherein the construct-derived exon further comprises a translatable coding sequence which is in-frame with coding sequence of the endogenous gene in the homologously recombinant cell.

126. The method of claim 125 wherein the translatable coding sequence is identical to the endogenous coding sequence in the first exon of the endogenous gene.

127. The method of claim 125 wherein the translatable coding sequence is different from the endogenous coding sequence in the first exon of the endogenous gene.

128. The method of claim 126, wherein the vertebrate cell is a primary or secondary cell.

129. The method of claim 128, wherein the primary or secondary cell is a mammalian cell.

130. The method of claim 128, wherein the primary or secondary cell is a human cell.

131. The method of claim 126, wherein the vertebrate cell is an immortalized cell.

132. The method of claim 131, wherein the immortalized cell is of mammalian origin.

133. The method of claim 131, wherein the immortalized cell is of human origin.

134. The method of claim 127, wherein the vertebrate cell is a primary or secondary cell.

135. The method of claim 134, wherein the primary or secondary cell is a mammalian cell.

136. The method of claim 134, wherein the primary or secondary cell is a human cell.

137. The method of claim 127, wherein the vertebrate cell is an immortalized cell.

138. The method of claim 137, wherein the immortalized cell is of mammalian origin.

139. The method of claim 137, wherein the immortalized cell is of human origin.

140. The method of claim 114, wherein the therapeutic product is a hormone.

141. The method of claim 114, wherein the therapeutic product is a cytokine.

142. The method of claim 114, wherein the therapeutic product is an enzyme.

143. The method of claim 114, wherein the therapeutic product is a clotting factor.

144. The method of claim 114, wherein the therapeutic product is selected from the group consisting of antigens, antibodies, transport proteins, receptors, regulatory proteins, structural proteins, transcription factors, and ribozymes.

145. The method of claim 114, wherein the therapeutic protein or glycoprotein is selected from the group consisting of calcitonin, insulinotropin, insulin-like growth factors, parathyroid hormone, β-interferon, nerve growth factors, TGF- β, tumor necrosis factor, glucagon, bone growth factor-2, bone growth factor-7, TSH- β, interleukin 1, interleukin 2, interleukin 3, interleukin 6, interleukin 11, interleukin 12, CSF-macrophage, CSF-granulocyte/macrophage, immunoglobulins, catalytic antibodies, protein kinase C, superoxide dismutase, tissue plasminogen activator, urokinase, antithrombin III, DNase, tyrosine hydroxylase, blood clotting factor V, blood clotting factor VII, blood clotting factor X, blood clotting factor XIII, apolipoprotein E, apolipoprotein A-I, globins, low density lipoprotein receptor, IL-2 receptor, IL-2 receptor antagonists, alpha-1 antitrypsin, immune response modifiers, soluble CD4, FSHβ, insulin, and thrombopoietin.

146. The method of claim 114, wherein the therapeutic product is α-interferon.

147. The method of claim 114, wherein the therapeutic product is α-galactosidase.

148. The method of claim 114, wherein the therapeutic product is glucocerebrosidase.

149. The method of claim 114, wherein the therapeutic product is blood clotting factor VIII.

150. The method of claim 114, wherein the therapeutic product is blood clotting factor IX.

151. The method of claim 114, wherein the therapeutic product is growth hormone.

152. The method of claim 114, wherein the therapeutic product is erythropoietin.

153. The method of claim 114, wherein the therapeutic product is β-interferon.

154. The method of claim 114, wherein the vertebrate cell is a mammalian fibroblast.

155. The method of claim 114, wherein the vertebrate cell is a primary or secondary cell of human fibroblast origin.

156. The method of claim 155, wherein the therapeutic product is human α-interferon.

157. The method of claim 155, wherein the therapeutic product is human β-interferon.

158. The method of claim 114, wherein the regulatory sequence comprises a constitutively active promoter.

159. The method of claim 114, wherein the regulatory sequence is a mouse metallothionein-1 promoter.

160. The method of claim 114, wherein the regulatory sequence is an actin promoter.

161. The method of claim 114, wherein the regulatory sequence is a collagen promoter.

162. The method of claim 114, wherein the homologously recombinant cell is, prior to introduction into the mammal, enclosed within a barrier device which permits passage of the therapeutic product from the interior of the barrier device to the exterior of the barrier device.

163. The method of claim 162, wherein the barrier device prevents the homologously recombinant cell from escaping the barrier device.

164. The method of claim 114, wherein

(1) the DNA construct further comprises a sequence encoding an amplifiable marker permitting selection of multiple copies of the sequence encoding the amplifiable marker, and

(2) the homologously recombinant cell of step (c) is cultured under conditions which select for cells having multiple copies of the sequence encoding the amplifiable marker, thereby coamplifying (i) the sequence encoding the amplifiable marker, (ii) coding sequence of the endogenous gene, and (iii) the exogenous regulatory sequence.

165. The method of claim 164, wherein the amplifiable marker is selected from the group consisting of dihydrofolate reductase, adenosine deaminase, and the trifunctional enzyme carbamoyl phosphate synthase-aspartate transcarbamylase-dihydroorotase (CAD).

166. The method of claim 164, wherein the vertebrate cell is of human origin.

167. The method of claim 164 wherein the vertebrate cell is a primary or secondary cell.

168. The method of claim 164 wherein the vertebrate cell is an immortalized cell.